

Bridging the Technology **Valley of Death**

in Joint Medical Development

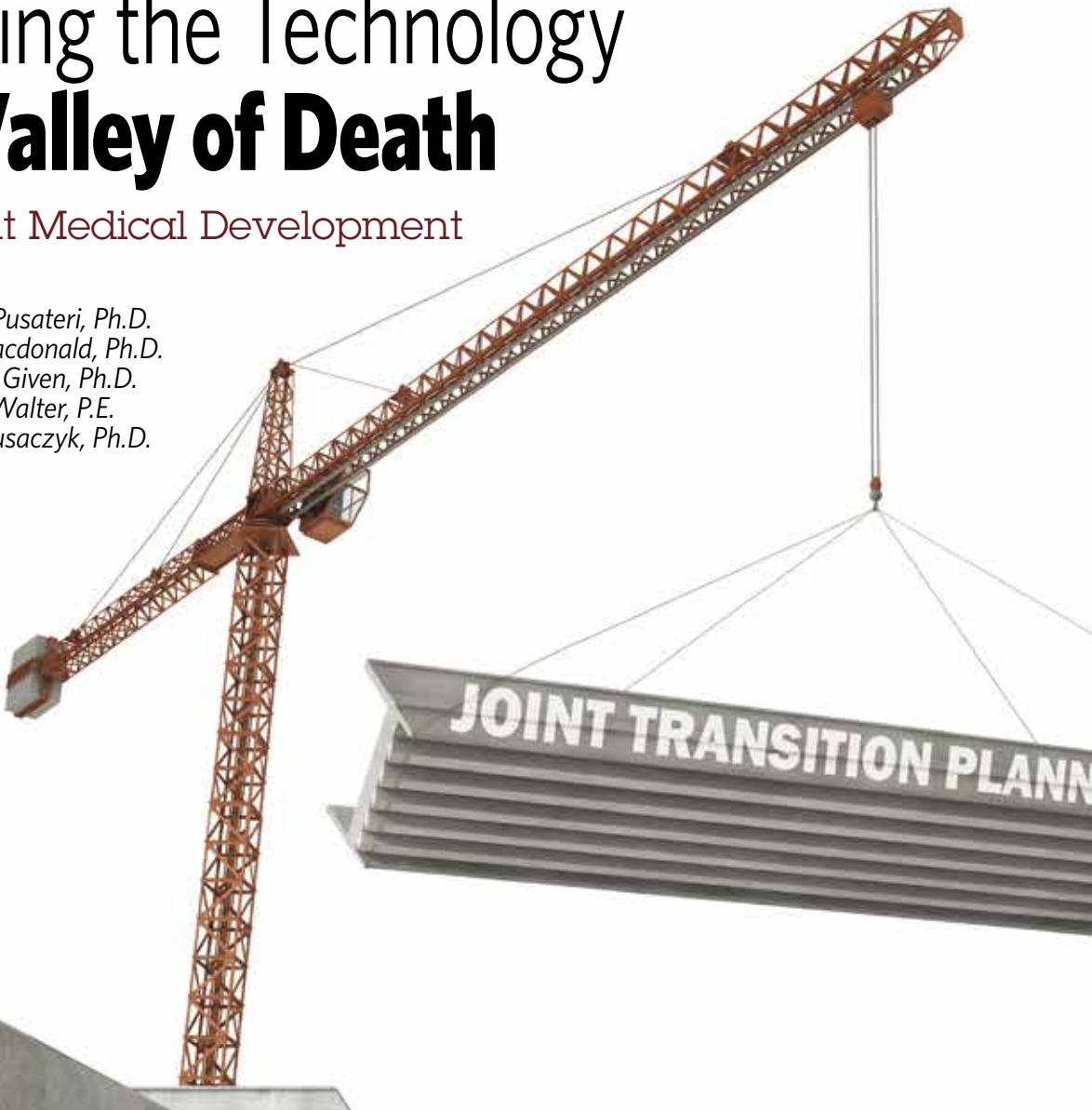
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One of the most difficult transitions in a product's life cycle is the transition from the science and technology (S&T) environment to advanced development (AD). Transition planning is necessary to bridge this technology "Valley of Death" in which promising technologies frequently are delayed or fail to make the transition. Without successful transitions, intellectual and financial investments in research do not translate to improved capabilities for the U.S. military. Early and thorough transition planning is key to success.

Transitions in medical product development traditionally have been conducted within the military Services, moving from a Service S&T program to its respective AD program. The launch of the Defense Health Program (DHP) in 2008 provided jointly managed resources to supplement and leverage existing individual Service research-and-development (R&D) investments and also provided the impetus to establish joint medical development portfolios.

In 2010, the Joint Program Committee for Combat Casualty Care established the Joint Hemorrhage and Resuscitation R&D Portfolio, which provided the first-ever comprehensive Department of Defense (DoD) view of the R&D pipeline for medical products that address bleeding, the leading cause of potentially preventable deaths on the battlefield (Eastridge et al., 2012). Initial pipeline review revealed several promising technologies in late S&T

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that did not have established transition pathways, Program Executive Office buy-in, or adequate funding. While there were significant opportunities to leverage funding and other resources across the DoD, no process had been established for joint transitions to medical AD. Therefore, our team, with input from a number of stakeholders and subject-matter experts (SMEs), developed a Joint Transition Planning Process that successfully facilitated transitions for seven programs.

Product Development “Valley of Death”

The transition from S&T to medical AD within DoD roughly parallels what has been termed the pharmaceutical or technology “Valley of Death.” The “Valley of Death” most frequently

FDA requirements. Some programs continue through Phase I clinical trials, while others may end before completion of preclinical development.

- Different Services have different procedures and expectations for transition.
- Stand-alone Service programs may not recognize opportunities to leverage funding or to fill joint (common) capability gaps.
- S&T teams often are not aware of the types of information and data needed for advanced developers to accept a program, or to enable entry into FDA regulated trials.
- Awareness, communication and coordination may be minimal among Service S&T and AD programs.



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refers to a lack of funding or development partners for a product to bridge the technology transition phase (Figure 1). This critical transition period spans from the late research, pre-materiel development decision (MDD) phase, through technology development. Specific activities during this phase for drugs or biologics products, for example, include: final proof of concept in relevant animal models; manufacturing development in accordance with Food and Drug Administration (FDA) Good Manufacturing Practices; analytical development; animal safety studies; initial clinical development planning; Investigational New Drug (IND) Application filing, first in human safety studies; and others. The proportion of these activities before transition to a chartered AD Integrated Product Team (IPT) depends on the Service sponsoring the S&T and the specifics of the program.

The most significant opportunity in developing a joint transition process for medical development programs is for Service S&T programs to directly transition into joint AD programs, with supplemental funding provided via the DHP. Joint programs provide an opportunity to systematically address capability gaps that are shared by all Services and to leverage Service funding and capabilities. A number of challenges also are apparent:

- S&T programs from various Services and agencies typically end at slightly different phases of research with respect to

Joint Transition Planning Process

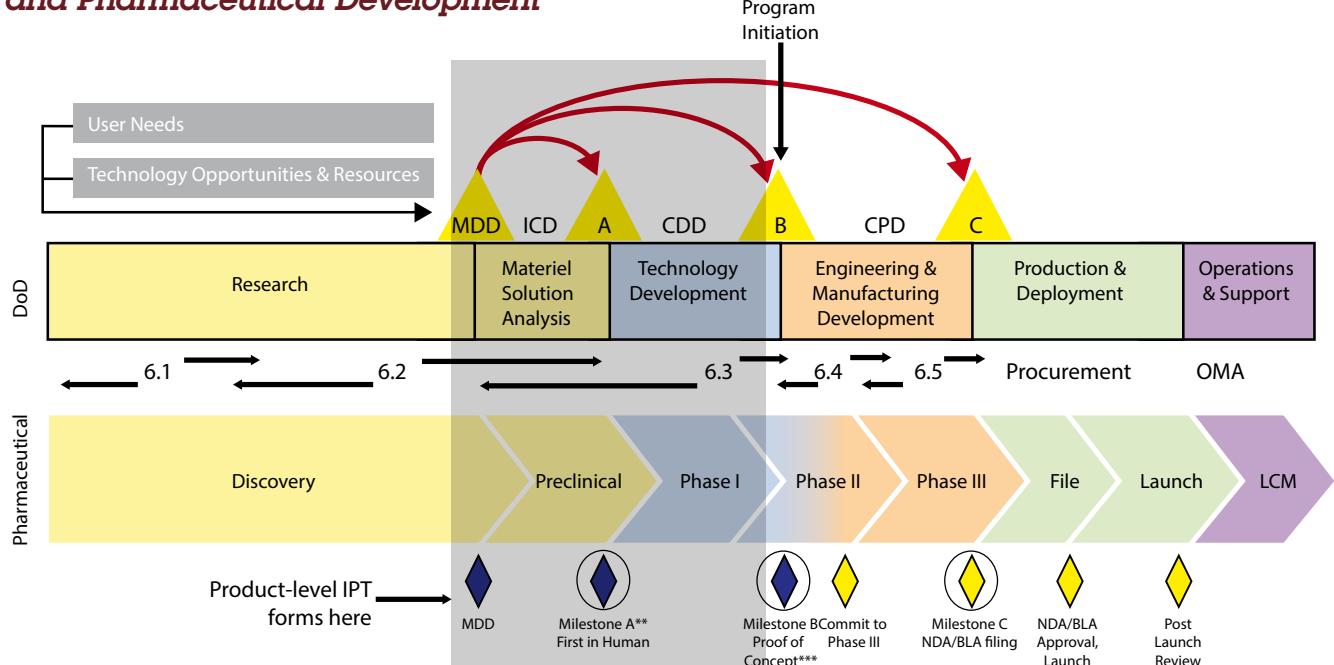
A Joint Transition Planning Process was developed to facilitate transitions involving different funding sources, different Service and agency paradigms for S&T, and different experiences with AD. This process helps bridge the technology development “Valley of Death” by facilitating and tailoring late-stage S&T to position the product for transition to AD and generating information useful in higher-level acquisition decisions. It complements but does not replace Service planning processes. It is important early in the process to reconcile development processes as much as possible across Services and to clarify lines of authority within different Service paradigms. Key components are the Joint Transition Planning Meeting and the Joint Transition Working Group (JTWG), and there is an overarching theme of communication.

Joint Transition Planning Meeting

The Joint Transition Planning Meeting provides a forum for S&T team presentation and a process for building advanced developer awareness. The meeting is structured to provide the following information and functions.

- Provide current product/program information.
- Provide information and assistance to the S&T team to prepare for transition.
- Assess potential for transition.
- Identify potential Service interest as AD lead.

Figure 1. DoD Medical Product Development Milestones and Pharmaceutical Development



Technology translation phase of “Valley of Death” is shown in the gray box.

Source: U.S. Army Medical Research and Materiel Command, Fort Detrick, Maryland, Decision Gate Office (Modified).

- Identify funding source(s).
- Understand Service(s) concurrence with importance of capability and approach.

Meeting preparation includes assisting and advising the S&T team and providing specific presentation content guidelines. The primary meeting outcomes are recommendations and may include identifying a lead advanced developer and funding commitment (subject to senior leader and milestone decision authority [MDA] approval) or formation of a JTWG to facilitate movement toward AD and a future reassessment. It also may be recommended that the S&T program continue in S&T or that it be discontinued due to lack of Service interest or funding.

The JTWG

A JTWG is formed to facilitate the transition of a promising S&T program to a joint AD program. The working group performs functions similar to those of an IPT for a limited period to bridge the gap until official designation of an AD lead, a chartered IPT and a formal AD program. The roles of the JTWG can be tailored to the needs of the specific program and transition situation.

Key functions and activities include the following as needed:

- Perform a detailed assessment of current program status (e.g., cost, schedule, regulatory, technical feasibility, risk analysis).

- Perform analysis of alternatives.
- Review the currently planned regulatory pathway and recommend potential changes.
- Determine status of requirements and acquisition documents and initiate production of documents.
- Assess current contracts and develop estimates for modifications and/or future contracts.
- Develop budget estimates and determine availability of funding.
- Develop an updated estimated timeline and work breakdown structure.
- Provide recommendations regarding a development decision.
- Assess relevant capability gaps, potential methods of employment and implications for an acquisition strategy.
- Assess relevance of the product for each Service.
- Assess security and/or status of intellectual property.
- Discuss the role of industry partners.

Early activities include an initial forming meeting, initiation of periodic meetings, an in-progress review (IPR) within 60 to 90 days, and establishment of electronic information sharing. Activities continue under the JTWG until either an advanced developer is designated and a chartered IPT formed or a decision is made not to continue the product into AD. Activities are tailored to provide the information needed to enable initial assessments, recommendations and decisions. The focus is on preparing for transition and enabling post-transition activities.

JTWG Membership

The JTWG is not an officially chartered body. Rather, it is a working group that technically functions as a subgroup of the joint portfolio-level steering committee. Core membership is augmented over time by additional experts and representatives. Membership includes representation from S&T team, Services or agencies, advanced developers, regulatory scientists and others as needed (e.g., requirements, budget, legal, contracting, cost estimating, scientific or user medical SMEs, logistics personnel).

Experience to Date

The process is flexible and structured sufficiently to ensure that the proper information is available to the appropriate groups to facilitate planning and decision making. Initially, there was significant controversy over what milestone decision process and what contracting and regulatory oversight office(s) to use, who would serve as

MDA, and other variables. While these were legitimate and important issues, they were largely due to the fact that the Defense Health Agency (DHA) was being established and the potential impact on procedural requirements was not yet clear. Each Service has established processes for within-Service transitions. The goal was not to establish new requirements to which programs must conform but to develop a process to move programs forward in a way that makes transitions compatible with entry into the AD processes already in place for each Service. The process has facilitated the progress of several products and also a decision to discontinue a program. Our experience to date includes:

2011—The Red Cell Pharming Program: This S&T program was sponsored by the Defense Advanced Research Projects Agency (DARPA) to develop a technology to produce universal red blood cells *in vitro* and to eliminate the need to collect red cells from donors. This would reduce logistical constraints and enhance the safety of blood transfusions. At the Joint Transition Planning Meeting, it was concluded that the projected unit cost for the “Pharmed” red cells was prohibitive. The program was not moved into AD. This promising technology now is being explored for other applications.

2012—Solvent Detergent Spray-Dried Plasma: This S&T program was sponsored by the Office of Naval Research (ONR) and Marine Corps Systems Command to produce a dried plasma that would reduce dramatically the logistical constraints associated with current frozen plasma. A dried product that could be rehydrated when needed would make it possible to provide plasma transfusions for combat casualties



DoD Solvent Detergent Spray-Dried Plasma in Development

Photo (with permission) by Entegris, Research Triangle Park, North Carolina.

wherever medically needed on the battlefield or in transport, as opposed to only where freezers and thawing equipment are present. This program was transitioned as the first Joint Medical Advanced Development Program chartered by DHA. The program was guided through the transition by a JTWG for more than a year, until an IPT was chartered. It is now a Navy-led, Joint Advanced Development Program, funded by DHP and Navy, with significant program support from the Air Force. This is part of a three-product U.S. Government strategy to develop dried plasma, including programs that incorporate different technological approaches and that are sponsored by the Army and the Biomedical Advanced Research and Development Authority (BARDA). Coordination is facilitated by IPT cross-membership.

2013—The Wound Stasis System: This DARPA program was designed to develop an expanding foam that could be infused into the abdominal cavity to control internal bleeding until the injured Service member could reach a surgeon. The program successfully advanced under the guidance of a JTWG and is now an Army-led, Joint Advanced Development Program, funded by DHP and the Army.

2013—Platelet Derived Hemostatic Agent: There were two competing technologies and development programs—one S&T program sponsored by Army and DARPA, the other by ONR. The goal was a product that could be infused intravenously to help stop bleeding. The recommendation from the Joint Transition Planning Meeting was to move both products forward for a later down-select, under an Army-led Joint Advanced Development Program. Subsequently, our interagency



DoD X-Stat Dressing to stop bleeding in deep wound tracks.

Photo (with permission) by RevMedx Inc., Wilsonville, Oregon.

partner, BARDA, agreed to develop one product, while the Army continued development of the other. The two programs are progressing with close-coordination and cross-membership on the IPTs. The DoD program is funded by DHP.

2013—Valproic Acid: This S&T program was sponsored by ONR to develop a drug that could be injected into a combat casualty to stabilize affected tissues and increase survival time before reaching surgery and blood transfusion. Following the Joint Transition Planning Meeting, a JTWG was formed and continues to move the program forward until a Navy-led Joint Advanced Development Program is established. The program continues with DHP and Navy funding and significant program support from the Air Force.

2013—Surviving Blood Loss Program: The goal of this DARPA S&T program was to develop a low-volume treatment that could be administered to bleeding casualties to increase survival time after severe blood loss. The research program developed a new drug—ethinyl estradiol-3-sulfate. At the Joint Transition Planning Meeting, it was determined that additional work was needed before any Service would be willing to commit to leading a Joint Advanced Development Team. Currently, the program is proceeding under the guidance of a JTWG in close coordination with DARPA and the participating DoD lab. Funding is provided by DHP and DARPA, and the program will be reassessed in a year.

2013—X-Stat Dressing: This product is the result of a S&T effort led by the U.S. Special Operations Command (USSOCOM) to develop a hemostatic dressing to stop bleeding from deep wound tracts in areas difficult to reach with standard dressings or tourniquets. A JTWG was formed and rapidly transitioned to a chartered IPT and an Army-led Joint Advanced Development Program. In addition to USSOCOM funding, the program has received important support from both the Air Force and the Army. The first-generation product has been FDA approved for battlefield use and has undergone limited fielding. The ongoing development program is aimed at gaining broader FDA approval and information on clinical use.

Status of the Process

Our process has met with a number of challenges and has been refined over time. Some aspects of developing the process and building support have been more difficult than anticipated. At times, some misunderstandings have caused controversy and resistance. During the first year or two when we were developing and implementing this process, there were concerns that we were trying to bypass established acquisition and milestone processes and to move programs forward without proper programmatic and contracting oversight. We addressed these concerns by increasing communication, by documenting our oversight processes, and by seeking additional guidance where needed.

Bringing the Services together to cooperate on programs has been easier than initially expected. The initial incentive for participation was the potential to leverage DHP funding. However, as the process evolved and achieved some early successes, a belief in the importance of the process seemed to dominate. In fact, after a recent budget cut, two projects were almost completely defunded in future years. Nonetheless, the JTWSGs continued to meet to try to move the programs forward. As it turned out, we were able to get partial funding restored, and the teams' interim work was not in vain.

In general, the process has greatly facilitated transitions to Joint Medical Advanced Development Programs, even while higher-level processes were being refined among DHA and the Services. The programs leverage DHP and Service resources and complement existing Service development programs.

The experience of our JTWSGs reinforces the importance of developing transition plans and joint multidisciplinary teams for each program. Transition planning should be initiated as early as possible at the portfolio level, as an S&T management function to ensure that the leading technologies are positioned properly for transition. In our experience, the portfolio-level perspective has enabled identification of top-level prioritizations and available funds from DHP and across Services. This portfolio approach facilitates leveraging and allows the targeting of resources toward the highest-priority programs that need to transition. These processes may be useful for other medical or nonmedical development programs.

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